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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,551	03/28/2000	Dorothy M. Morre'	8951-124-999	5585

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EXAMINER

WELLS, LAUREN Q

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 06/07/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/536,551

Applicant(s)

MORRE ET AL.

Examiner

Lauren Q Wells

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 12-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

Claims 12-24 are pending. The Amendment filed March 14, 2002, amended claims 12, 14, 15 and 17-24, and cancelled claims 1-11 and 25-54. The formal drawings filed March 14, 2002, Paper No. 12 have been received.

#### ***Response to Arguments and 1.132 Declaration***

The declaration under 37 CFR 1.132 filed March 14, 2002, is sufficient to overcome the rejection of claims 12-24, as the Biofactors reference in the 103(a) rejection in the previous Office Action, is the Applicant's own work.

Applicant's arguments with respect to claims 12-24 have been considered but are moot in view of the new ground(s) of rejection.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies, does not reasonably provide enablement for test substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court

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in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

In the instant case, an incredible amount of experimentation would be required to discover every possible chemical compound that binds to AR-NOX. While the specification recites the use of antibodies as test substances, the specification is silent regarding other possible test substances. Furthermore, the working examples of the instant specification are directed toward screening methods, wherein antibodies are the test substances. While it is within the skill of one in the art to utilize antibodies as test substances for AR-NOX, it would not be within the skill of one in the art to utilize other compounds as test substances. See US Patent No. 5,605,810, wherein it is disclosed that antibodies are known test agents for AR-NOX. The prior art is silent regarding additional test substances for AR-NOX.

Hence, the instant invention lacks enablement for test substances.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 12-16 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morre et al. (5,605,810) in view of Wheelock et al. (6,140,063) in further view of Asard et al. (Plas. Mem. Redox. Systems).

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Morre et al. teach NADH oxidase as a target for a variety of uses in diagnosis and therapy. Conjugating antibodies with labels for detection of NADH oxidase is disclosed. In assaying for NADH oxidase activity, it is disclosed that one may measure the rate of disappearance of NADH, the appearance of NAD or the rate of appearance or disappearance of a reaction product or reactant. Further, it is disclosed that since the NADH oxidase appears to be associated with growth of cells, inhibiting the NADH oxidase activity serves as a cytostatic agent, resulting in apoptosis. Assays for identifying NADH oxidase are disclosed, wherein an ascorbate radical is disclosed as a measure of NADH oxidase activity. The reference lacks exemplification of a method of screening and ubiquinone. See Col. 1, lines 55-Col. 2, line 2; Col. 4, line 10-Col. 6, line 54; Col. 8, lines 4-10.

Wheelock et al. teach that testing compounds that inhibit biochemical functions for treating diseases is known in the art. See abstract; Col. 1, line 17-Col. 7, line 30.

Asard et al. teach plasma membrane redox systems and their role in biological stress and disease. It is disclosed that co-enzyme Q, which is synonymous to quinone, functions as an electron donor for NADH oxidase. It is further disclosed that a stoichiometric relationship exists between NADH oxidation, protein disulfide reduction and protein thiol oxidation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Morre et al. with those of Wheelock et al. and obtain a method of screening agents that sequester NADH oxidase because a) Morre et al. teach that inhibitors of NADH oxidase are known and are useful in treating diseases such as cancer; b) Morre et al. teach that it is known to label compound to detect their activity in the presence of NADH oxidase; thus, since labeling compounds that interact with NADH oxidase is known,

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since NAHD inhibitors are known to have therapeutic benefits, and since testing compounds that inhibit biochemical functions is known, it would be within the skill of one of ordinary skill to use the teachings of Morre et al. in combination with those of Wheelock et al. to develop a method of screening compounds that inhibit NADH oxidase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Asard et al. with that of the combined references and obtain a method of screening wherein ubiquinone is a positive control because a) Asard et al. teach that ubiquinone is known to function as an electron donor for NADH oxidase; hence, the oxidation state of ubiquinone can serve as a baseline for NADH oxidase activity.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morre et al. in view of Wheelock et al. in further view of Asard et al.

Morre et al. is applied as discussed above. The reference lacks an exemplification of screening and measuring the disulfide-thiol interchange activity.

Wheelock et al. is applied as discussed above.

Asard et al. is applied as discussed above.

Morre et al. and Wheelock et al. are combined as discussed above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Asard et al. with that of the combined references and obtain a method of screening wherein the presence of disulfide-thiol interchange in the substrate is detected because a) Asard et al. teach that the activity of the disulfide-thiol interchange is directly correlated to the activity of NADH oxidase activity; hence, the interchange can serve as a measure of NADH oxidase activity.

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Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morre et al. in view of Wheelock et al. in further view of Garrett et al. (Biochemistry).

Morre et al. is applied as discussed above. The reference lacks exemplification of a method of screening, cytochrome c, and a reactive oxygen species.

Wheelock et al. is applied as discussed above.

Garrett et al. disclose the biochemical workings of the electron transport chain, wherein the integral relationship between a superoxide dimutase, cytochrome c, and NADH oxidase is disclosed. See pages 632-658.

Morre et al. and Wheelock et al. are combined as discussed above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the combined references with those of Garrett et al. and obtain a method of screen for agents that inhibit NADH oxidase by incubating a mixture comprising NADH oxidase, a test agent, cytochrome c, and a substrate capable of generating oxygen species because a) Garrett et al. teach that the reduction of cytochrome c is dependent upon a superoxide dimutase and that the reduction of the superoxide dimutase is dependent on NADH oxidase; hence, measuring the activity of NADH oxidase by measuring the activity of cytochrome c would be within the skill of one in the art.

### ***Unexpected Results***

It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972).

In the instant case, there are no unexpected results.

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***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on T-F (6-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw  
May 28, 2002

  
RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200